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EXAMINER	
SITTON, JEHANNE SOUAYA	
ART UNIT	**PAPER NUMBER**
1634	

DATE MAILED: 12/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/508,658	KROHN ET AL.	
	Examiner	Art Unit	
	Jehanne S. Sitton	1634	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 September 2005*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *9-35* is/are pending in the application.

4a) Of the above claim(s) *9-22,24 and 28-34* is/are withdrawn from consideration.

5)☒ Claim(s) *27* is/are allowed.

6)☒ Claim(s) *23,25,26 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 March 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Currently, claims 8-24 and newly added claims 25-35 are pending in the instant application. Claims 8-22, 24, and 28-34 are withdrawn from consideration as being drawn to non elected inventions. Claims 23, 25-27, and 35 are under consideration at this time. The amendments and arguments have been thoroughly reviewed but were not found sufficient to place the instant application in condition for allowance. As the instant application is not in condition for allowance, no claims from non elected inventions have been rejoined. The following rejections are either reiterated, or newly applied. This is action is NON-FINAL.

2. Newly submitted claims 28-34 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: the claims are directed to protein sequences, which were placed in a different group in the restriction requirement set forth in the previous office action.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 28-34 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Interview

3. In the interview dated August 2, 2005, the examiner and applicant's representative discussed rejoinder of claims to proteins. The examiner indicated that depending on allowable subject matter, protein claims may be rejoined. As all the pending claims are not in condition for

allowance, the examiner has not rejoined claims directed to proteins. HOWEVER, regarding protein claims, at the time of the interview, the examiner was unaware of the impending issue of US Patent 6,951,928 to Peltonen et al. The '928 patent teaches a nucleic acid SEQ ID NO: 1, which differs from instant SEQ ID NO: 1 in that instantly claimed SEQ ID NO: 1 contains 16 extra nucleotides on the 5' end which are not disclosed in the sequence of the '928 patent, as well as a polymorphism which does not alter the sequence of SEQ ID NO: 2 (see sequence listing). However, the protein of SEQ ID NO: 2 taught by '928 is identical to the protein of SEQ ID NO: 2 of the instant application. It is further noted that the '928 patent teaches a mutation which is a C to T substitution at position 889 of SEQ ID NO: 1 of '928 which would encode a premature stop codon at codon 257 of the protein encoded by the sequence, as well as an A to G substitution at position 374 of SEQ ID NO: 1 of '928 which would encode a K to L substitution at codon 83 (see col. 6, lines 1-5). Further, see claims 1-16 of '928.

4. The following office action is made NON-Final, as the examiner erroneously indicated that claims directed to any nucleic acid sequence which encoded the particular mutations listed in the specification were allowable.

New Grounds of Rejection

Claim Rejections - 35 USC § 112

5. Claims 23, 25, 26, and 35 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an isolated nucleic acid molecule comprising SEQ ID NO: 1, an isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at

position 905 is a T instead of a C, and an isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at position 383 is a G instead of an A, does not reasonably provide enablement for nucleic acids encoding variants of SEQ ID NO: 1 which include a mutation responsible for APECED wherein the mutation results in R257X mutation in the protein encoded by SEQ ID NO: 1, or wherein the mutation results in "K42E" mutation in the protein encoded by SEQ ID NO: 1, or a functionally equivalent isolated DNA sequence hybridizable thereto or the protein of claim 5, or sequences hybridizable to any of such nucleic acids. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims. There are many factors to be considered when determining whether there is sufficient evidence to support determination that a disclosure does not satisfy the enablement requirements and whether any necessary experimentation is undue. These factors have been described by the court in *In re Wands*, 8 USPQ2d 1400 (CA FC 1988). *Wands* states at page 1404,

> "Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in Ex parte Forman. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims."

The claims are broadly drawn to nucleic acids from any source which are variants of SEQ ID NO: 1 and "include" (considered open language in that more mutations are encompassed in SEQ ID NO; 1) a mutation responsible for APECED wherein the mutation is R257X or "K42E", functionally equivalent DNA hybridizable thereto, as well as generally to sequences which would hybridize thereto (claims 23 and 35). The claims therefore encompass sequences from

any source which are "variants" of SEQ ID NO: 1 and contain any insertion, deletion or missense mutation, as well as the mutations listed in the claim, which have not been taught in the specification. Additionally, given the addition of new claims 29, 30 and 33-34, it is clear that the term "variant" is not limited to a molecule with the full length of SEQ ID NO: 1 as claims 33 and 34 only require a single structural motif in the molecule of claims 29 or 30.

The specification teaches that SEQ ID NO: 1 is a gene encoding a protein associated with Autoimmune polyglandular syndrome type I (APS I), also known as autoimmune polyendocrinopathy-candidiasis-ectodermal dystrophy (APECED). The specification teaches that this protein is known in the art as AIRE (encoded by SEQ ID NO: 1). The specification further teaches finding 2 splice variants of this protein, AIR-2 and AIR-3 were found. It is unclear which nucleic acids encode AIR 2 and AIR 3. The specification teaches that mutations were found in AIR 1, exon 2: K42E, and exon 6: R257X in 2 patients, respectively, with APECED but not in healthy controls. The specification, however, teaches that no mutations were found in either AIR2 or AIR3. The specification teaches that AIR 1 has certain domains found in other proteins, such as two PHD finger motifs, a proline rich region, and an LXXLL motif (see page 9). The specification, however, does not teach or demonstrate the specific functions or biological activity for the AIR1 protein, the protein encoded by SEQ ID NO: 1.

At the time the invention was filed, the prior art was silent with respect to the function for the protein encoded by SEQ ID NO: 1. Neither the art nor the specification provide any assay for detecting or assaying the function of such proteins. Even the postfiling date art of Su (Su et al; Current Opinion in Immunology, vol. 16, pp 746-752, 2004) teaches that the molecular mechanisms by which AIRE functions are not well understood (see abstract). Su teaches that

while Aire appears to have a role in central tolerance by upregulating the expression of organ specific antigens in the thymus, several key questions remain regarding this mechanism, including on the molecular level (see page 750, col. 2). Further, while the post filing date art teaches of additional mutations in Aire (see Aaltonen et al; Nature Genetics, vol. 17, 1997, pp 399-403), the mutations in Aire taught by Aaltonen all result in prematurely truncated proteins. Aaltonen teaches that silent C to T polymorphisms were found in the nucleic acid sequence. These polymorphisms do not seem to be associated with disease. Aaltonen does not provide any guidance as to which missense mutations would be predictably correlated with disease, nor which portions of the protein are required for loss of function mutations which would be associated with disease.

It is further noted that while the specification continually refers to the "K42E" mutation, the number system used for the mutation at codon position 42 is unclear. The sequence listing lists the first ATG beginning at position 137 of SEQ ID NO: 1, as the first codon. Looking at Figure 3A, the sequence of GTTCGAG can be found at positions 902-908 of SEQ ID NO: 1, such that the Arg to X mutation occurs at codon 257, given that positions 137-139 of SEQ ID NO: 1 are the start codon. HOWEVER, this numbering system does not apply to the "K42E" mutation. Using Figure 3C, the sequence GTTCAAGG is found at positions 379-386 of SEQ ID NO: 1 (the A to G mutation occurs at position 383 of SEQ ID NO: 1) which does not correspond to codon 42 if the start codon begins at position 137 of SEQ ID NO: 1. Accordingly, the specification does not appear to enable an association with a mutation labeled as "K42E".

The claimed "variant includes" recitation encompasses any number of additional variations in SEQ ID NO: 1, however the skilled artisan would have no way of determining what

constituted "a variant" of SEQ ID NO: 1, as opposed to an unrelated molecule. The specification has only taught 2 mutations which are associated with APECED. Neither the specification nor the art teach which regions of the encoded polypeptide are required for the activity or function of the polypeptide encoded by SEQ ID NO: 1. While the specification sets forth domains and motifs included within this polypeptide, as acknowledged by the specification, such domains are found in a large number of unrelated proteins, which have no association with APECED. Neither the specification nor the art at the time of filing provide a universal correlation between any mutation or polymorphism in SEQ ID NO: 1 and a predictable diagnosis of APECED. Therefore, the skilled artisan would be required to perform undue experimentation to identify which mutations were responsible for APECED. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which mutations were responsible for disease. Accordingly, given the lack of teaching of function for the protein of SEQ ID NO: 2, or how the mutations R257X or "K42E" affect the function of SEQ ID NO: 2, the skilled artisan would not be able to predictably determine what other mutations in SEQ ID NO: 1 would be responsible for APECED

Additionally, the claims are not enabled for nucleic acids which are functionally equivalent isolated DNA sequences hybridizable to SEQ ID NO: 1 or variants of SEQ ID NO: 1. The specification has taught a polypeptide of SEQ ID NO: 2, however the specification has not taught the activity or function of the polypeptide, nor where and how to modify the polypeptide to produce a protein or variant with the same functionality. The specification has not taught which portions of a putative polypeptide would be associated with APECED. The instant claims are drawn to undisclosed sequences encoding *any* number of additional modification that have

not been contemplated. While the specification teaches the amino acid sequence of SEQ ID NO: 2, one sequence does not enable a genus of polypeptide molecules based on the limited information disclosed in instant application. Therefore, the skilled artisan would be required to perform undue experimentation to make functionally equivalent isolated DNA sequences hybridizable thereto. The skilled artisan would have no way of knowing which nucleic acid sequences encoded functional variants of SEQ ID NO: 2 because the specification does not provide a description of the nucleotide or amino acid sequences which constitute these functional variants. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for its activity.

Thus given the broad claims in an art whose nature is identified as unpredictable, the unpredictability of that art, the large quantity of research required to define these unpredictable variables, the lack of guidance provided in the specification, the absence of a working example and the negative teachings in the prior art balanced only against the high skill level in the art, it is the position of the examiner that it would require undue experimentation for one of skill in the art to make and use the claims as broadly written.

6. Claims 23, 25, 26, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to nucleic acids from any source which are variants of SEQ ID NO: 1 and "include" (considered open language in that more mutations are encompassed in SEQ ID NO; 1) a mutation responsible for APECED wherein the mutation is R257X or "K42E", functionally equivalent DNA hybridizable thereto, as well as generally to sequences which would hybridize thereto (claims 23 and 35). The claims therefore encompass sequences from any source which are "variants" of SEQ ID NO: 1 and contain any insertion, deletion or missense mutation, as well as the mutations listed in the claim, which have not been taught in the specification. Additionally, given the addition of new claims 29, 30 and 33-34, it is clear that the term "variant" is not limited to a molecule with the full length of SEQ ID NO: 1 as claims 33 and 34 only require a single structural motif in the molecule of claims 29 or 30.

The specification teaches that SEQ ID NO: 2 has certain domains found in other proteins, such as two PHD finger motifs, a proline rich region, and an LXXLL motif (see page 9). The specification, however, does not teach or demonstrate the specific functions or biological activity for the AIR1 protein (SEQ ID NO: 2), the protein encoded by SEQ ID NO: 1. At the time the invention was filed, the prior art was silent with respect to the function for the protein encoded by SEQ ID NO: 1. Neither the art nor the specification provide any assay for detecting or assaying the function of such proteins. Even the postfiling date art of Su (Su et al; Current Opinion in Immunology, vol. 16, pp 746-752, 2004) teaches that the molecular mechanisms by which AIRE functions are not well understood (see abstract). Su teaches that while Aire appears to have a role in central tolerance by upregulating the expression of organ specific antigens in the thymus, several key questions remain regarding this mechanism, including on the molecular level (see page 750, col. 2).

The claimed "variant includes" recitation encompasses any number of additional variations in SEQ ID NO: 1, however the skilled artisan would have no way of determining what constituted "a variant" of SEQ ID NO: 1, as opposed to an unrelated molecule. The specification has only taught 2 mutations which are associated with APECED. Neither the specification nor the art teach which regions of the encoded polypeptide are required for the activity or function of the polypeptide encoded by SEQ ID NO: 1. While the specification sets forth domains and motifs included within this polypeptide, as acknowledged by the specification, such domains are found in a large number of unrelated proteins, which have no association with APECED. Neither the specification nor the art at the time of filing provide a universal correlation between any mutation or polymorphism in SEQ ID NO: 1 and a predictable diagnosis of APECED. Accordingly, given the lack of teaching of a structure/function correlation for the protein of SEQ ID NO: 2, or how the mutations R257X or "K42E" affect the function of SEQ ID NO: 2 or are correlated to APECED, the skilled artisan would not be able to determine what other mutations in SEQ ID NO: 1 would be responsible for APECED.

Additionally, the specification fails to describe a sufficient number of species of the broadly claimed genus of nucleic acids which are functionally equivalent isolated DNA sequences hybridizable to SEQ ID NO: 1 or variants of SEQ ID NO: 1. The specification has taught a polypeptide of SEQ ID NO: 2, however the specification has not taught the activity or function of the polypeptide, nor where and how to modify the polypeptide to produce a protein or variant with the same functionality. The specification has not taught which portions of a putative polypeptide would be associated with APECED. The instant claims are drawn to undisclosed sequences encoding *any* number of additional modifications that have not been

contemplated. While the specification teaches the amino acid sequence of SEQ ID NO: 2, one sequence does not describe a genus of polypeptide molecules based on the limited information disclosed in instant application. The skilled artisan would have no way of knowing which nucleic acid sequences encoded functional variants of SEQ ID NO: 2 because the specification does not provide a description of the nucleotide or amino acid sequences which constitute these functional variants. The skilled artisan would be required to perform manipulations and extensive modification of the protein to determine where and how to make modifications to determine which fragments of the polypeptide were responsible for its activity.

It is further noted that while the specification continually refers to the "K42E" mutation, the number system used for the mutation at codon position 42 is unclear. The sequence listing lists the first ATG beginning at position 137 of SEQ ID NO: 1, as the first codon. Looking at Figure 3A, the sequence of GTTCGAG can be found at positions 902-908 of SEQ ID NO: 1, such that the Arg to X mutation occurs at codon 257, given that positions 137-139 of SEQ ID NO: 1 are the start codon. HOWEVER, this numbering system does not apply to the "K42E" mutation. Using Figure 3C, the sequence GTTCAAGG is found at positions 379-386 of SEQ ID NO: 1 (the A to G mutation occurs at position 383 of SEQ ID NO: 1) which does not correspond to codon 42 if the start codon begins at position 137 of SEQ ID NO: 1. Accordingly, from the disclosure in the specification, the specification fails to convey to one of skill in the art that applicants were in possession of a protein of SEQ ID NO: 2 with a K to L substitution at amino acid position 42.

The claims are directed to a broad genus of nucleic acids for which a representative number of species have not been described by the specification. The claimed genus of nucleic

acids includes variants of SEQ ID NO: 1 which have not been taught or described by the specification. For example, the post filing date art teaches of additional mutations in Aire (see Aaltonen et al; Nature Genetics, vol. 17, 1997, pp 399-403). Further, Aaltonen teaches that silent C to T polymorphisms were found in the nucleic acid sequence. These variations have not been taught or described by the specification. It is further noted that US Patent 6,951, 928 teaches and claims a number of mutations found in a nucleic acid encoding a protein identical to SEQ ID NO: 2, which have not been taught or described by the instant specification. As no structure/function correlation is taught with regard to the structure of SEQ ID NO: 1 or 2, or how mutations in such are associated with APECED, the specification fails to provide adequate description of the broad variable genus encompassed by the claims.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

With the exception of SEQ ID NOS: 1, an isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at position 905 is a T instead of a C, and an isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at position 383 is a G instead of an A, the skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides and/or proteins, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is

part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993), and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence.

Finally, University of California v. Eli Lilly and Co., 43 USPQ2d 1398, 1404, 1405 held that:

To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (1997); In re Gosteli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) (" [T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966.

An adequate written description of a DNA, such as the cDNA of the recombinant plasmids and microorganisms of the '525 patent, "requires a precise definition, such as by structure, formula, chemical name, or physical properties," not a mere wish or plan for obtaining the claimed chemical invention. Fiers v. Revel, 984 F.2d 1164, 1171, 25 USPQ2d 1601, 1606 (Fed. Cir. 1993). Accordingly, "an adequate written description of a DNA requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it; what is required is a description of the DNA itself." Id. at 1170, 25 USPQ2d at 1606.

7. Claims 23, 25, 26, and 35 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a New Matter Rejection.

The claimed recitation of "said mutation resulting in [R257X, K42E] mutation in the protein encoded by SEQ ID NO: 1, encompasses degenerate codons in SEQ ID NO: 1 which encode the recited mutations. However, the specification and claims as originally filed fail to provide specific support for nucleic acids encoding the protein of SEQ ID NO: 2, nor do they

provide support for degenerate codons of specific mutations. At Figure 3, the specification only provides the specific nucleic acid sequences which are responsible for the R257X and "K42E" mutations (C to T, G to A, respectively). Further, at page 8, when referencing the R257X and "K42E" mutations, the specification provides the specific codon changes for each (CGA to TGA; AAG to GAG respectively). Also, when referring to detection of such mutations, the specification teaches that such mutations can be detected because the R257X mutation destroys a TaqI restriction site and the "K42E" mutation introduces a novel TaqI site. The specification provides no teaching of detection of such mutations using degenerate codons. Accordingly, the recitation appears to introduce new matter into the instantly claimed invention.

Indefinite

8. Claim 23 and newly added claims 26 and 35 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 and newly added claim 35 are indefinite in the phrase "characterized in comprising" as it is unclear if the recitation refers to the claimed reagent or the DNA it reacts with. Accordingly, the metes and bounds of the claim are unclear. The response asserts that claim 23 has been canceled rendering this rejection moot. It is noted, however, that the claim is still pending, that newly added claim 35 recites the phrase. The rejection is therefore maintained and newly applied to claim 35.

Claims 26 and 35 are indefinite in the number system used for the mutation at codon position 42. The sequence listing lists the first ATG beginning at position 137 of SEQ ID NO: 1,

as the first codon. Looking at Figure 3A, the sequence of GTTCGAG can be found at positions 902-908 of SEQ ID NO: 1, such that the Arg to X mutation occurs at codon 257, given that positons 137-139 of SEQ ID NO: 1 are the start codon. HOWEVER, this numbering system does not apply to the "K42E" mutation. Using Figure 3C, the sequence GTTCAAGG is found at positions 379-386 of SEQ ID NO: 1 (the A to G mutation occurs at position 383 of SEQ ID NO: 1) which does not correspond to codon 42 if the start codon begins at position 137 of SEQ ID NO: 1. Accordingly, the metes and bounds of position "42" with respect to SEQ ID NO: 1 is indefinite and the metes and bounds of the claims are unclear.

Claim 26 is indefinite in the recitation of "or the protein of claim 5 or with reagents therewith" as it is unclear whether the claim is drawn to a protein. Further, claim 5 is cancelled; therefore it is unclear which protein is being referred to. Also, the recitation of "reagents therewith" is unclear because it cannot be determined if the claimed nucleic acid contains "reagents therewith", and if so, what reagents. Also, it is unclear whether this language further limits the preceding recitation of "an functionally equivalent isolated DNA sequence hybridizable thereto".

Claim Rejections - 35 USC § 102

9. Claims 23, 25, and 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Kim (Kim et al; PNAS, vol. 93, pages 15299-15304, 1996).

Kim teaches a nucleic acid sequence which contains a PHD finger and is thus considered a functionally equivalent of isolated DNA sequence hybridizable to SEQ ID NO: 1. As the claim does not recite what "functional activity" is encompassed, the recitation of a PHD finger domain,

which is found in SEQ ID NO: 1, is broadly interpreted as "functionally equivalent". With regard to claims 23 and 35, such sequence is hybridizable to SEQ ID NO: 1 or a variant and therefore "reacts" with such DNA.

10. Claims 23, 25, 26, 35 are rejected under 35 U.S.C. 102(b) as being anticipated by Brennan (US Patent 5,474,796).

Brennan teaches constructing all possible 10 mer nucleic acid sequences (see cols. 9 and 10). The nucleic acid sequences of Brennan are fragments of SEQ ID NOS 1 and the complement of SEQ ID NO: 1, as well as variants of SEQ ID NO: 1 including any mutation. Accordingly, such sequences are hybridizable to the complement of any of such sequences and would react with such sequences. With regard to claim 26, given the addition of new claims 29, 30 and 33-34, it is clear that the term "variant" is not limited to a molecule with the full length of SEQ ID NO: 1 as claims 33 and 34 only require a single structural motif in the molecule of claims 29 or 30. Accordingly, the term variant has been broadly interpreted to encompass sequences with variations of SEQ ID NO: 1, which are smaller in length than SEQ ID NO: 1.

Conclusion

11. Claim 27 is allowable.

12. The following claim recitation would also be allowable:

An isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at position 905 is a T instead of a C.

An isolated nucleic acid molecule comprising SEQ ID NO: 1 wherein the nucleotide at position is 383 a G instead of an A.

It is noted that an alignment of the specific sequences listed in Figure 3 with SEQ ID NO: 1 reveals that the designation of "K42E" mutation appears to be in error, and that instead, the A to G mutation appears to occur at position 383 of SEQ ID NO:1 as it is the only portion of SEQ ID NO: 1 that aligns with the GTTCAAGG sequence listed in Figure 3c. One of skill in the art would be able to determine this error based on the data listed in Figure 3, as well as the sequence of SEQ ID NO: 1, both provided in the originally filed specification.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to examiner Jehanne Sitton whose telephone number is (571) 272-0752. The examiner can normally be reached Monday-Thursday from 8:00 AM to 5:00 PM and on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (571) 272-0745. The fax phone number for this Group is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Jehanne Sitton
Primary Examiner
Art Unit 1634

Jehanne Sitth
12/21/05